

ABSTRACT

Dysphagia is a clinically significant toxicity after head and neck cancer (HNC) re-irradiation (re-RT). Accurate prediction models are needed to identify high-risk patients and support treatment planning. This study developed interpretable machine learning models to predict dysphagia following a second course of radiotherapy.

A retrospective cohort of 46 recurrent HNC patients treated with re-RT was analyzed. Dysphagia after re-RT was dichotomized as grade ≥ 2 versus grade < 2 according to CTCAE criteria. Clinical features included tumor stage, prior and re-RT prescription doses, treatment interval, and baseline dysphagia status. Dosimetric features were derived from cumulative dose distributions and converted to EQD2. Logistic regression (LR) was used as the primary interpretable model, with explainable boosting machine and decision tree models evaluated for comparison. Model performance was assessed using five-fold cross-validation and area under the receiver operating characteristic curve (AUC). LR achieved the best performance with a cross-validated AUC of 0.755. Parotid gland volume was the strongest predictor of dysphagia, while cumulative dose, laryngeal dose and volume, parotid dose metrics, fractionation, and treatment interval also contributed to prediction. More complex models did not improve performance compared with LR (AUC <0.700), likely due to the limited cohort size.

Interpretable machine learning models demonstrated clinically meaningful performance for predicting dysphagia after HNC re-RT. The identified predictors highlight the importance of cumulative dose burden and injury to salivary and laryngeal structures, supporting transparent AI approaches for toxicity risk stratification and treatment planning.

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Prediction of dysphagia after head and neck re-irradiation using interpretable machine learning models

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INTRODUCTION

Re-irradiation is a key treatment option for recurrent head and neck cancer (HNC), yet dysphagia remains a common and clinically significant toxicity. Existing predictive approaches often rely on simplified dose–response assumptions, limiting both accuracy and clinical interpretability.

This study presents an interpretable modeling framework for predicting dysphagia following a second course of radiation therapy, emphasizing cumulative dosimetric and anatomical features as the primary predictors. By focusing on transparency and clinical relevance, this approach enables meaningful risk stratification to guide treatment planning in heterogeneous re-irradiation scenarios.

A logistic regression (LR) model with built-in feature selection method implemented using the InterpretML framework (<https://github.com/interpretml/interpret>) was used as the primary predictive model. An explainable boosting machine (EBM) and a decision tree (DT) model were trained as comparison models using the same feature set. Model performance was evaluated using five-fold cross-validation and receiver operating characteristic (ROC) analysis.

RESULTS

Fig. 1 shows the ROC curves comparing LR, EBM, and DT models. Logistic regression achieved the highest predictive performance, with a mean cross-validated area under the curve (AUC) of 0.755, outperforming the more complex models in this cohort.

Fig. 2 visualizes the parameter weights of the logistic regression model. Dosimetric and anatomical factors dominated the model, with right parotid gland volume emerging as the most influential predictor of dysphagia following re-irradiation. Additional high-ranking features included maximum cumulative dose, larynx maximum dose, and re-irradiation fractionation, highlighting the importance of cumulative dose burden and laryngeal dose exposure in dysphagia risk. Laryngeal anatomical and dosimetric metrics, including larynx volume and larynx D1cc, also contributed substantially, reinforcing the clinical relevance of laryngeal sparing in the re-irradiation setting. Parotid-related dose and volume metrics from both sides, as well as treatment duration, demonstrated moderate importance.

Discussion

The results suggest that dysphagia following HNC re-RT is primarily driven by cumulative dose burden and injury to salivary and laryngeal structures, with parotid gland volume and laryngeal dose emerging as key predictive factors. The proposed interpretable LR model demonstrates potential for clinically meaningful risk stratification and underscores the value of transparent modeling approaches for toxicity prediction in re-RT settings. Future efforts will focus on expanding the cohort size through additional institutional data to improve model robustness and generalizability.

Table 1. Patient and Treatment Characteristics (N = 46).

Characteristic	Value	Characteristic	Value
Age at re-RT (years)	61.2 $\pm$ 14.6 (range: 28–90)	Nodal stage at re-irradiation	
Sex		n0	17 (37%)
male	29 (63%)	N1–n3	29 (63%)
female	17 (37%)	Chemotherapy during first rt	
Smoking history		Yes	30 (65%)
current smoker	4 (9%)	No	16 (35%)
non-smoker	21 (46%)	Surgery before first rt	
previous smoker	21 (46%)	Yes	21 (46%)
HPV status		No	25 (54%)
positive	6 (13%)	Dysphagia after first rt (grade ≥ 2)	11 (24%)
negative	40 (87%)	Interval between rt courses (years)	2.5 (range: 0.2–20.1)
T stage at re-RT		Chemotherapy during re-irradiation	26 (57%)
t1–t2	20 (43%)	Surgery before re-irradiation	26 (57%)
t3–t4	26 (57%)	Second-treatment dysphagia (grade ≥ 2)	13 (28%)

METHODS AND MATERIALS

Under IRB approval, A retrospective cohort of 46 patients with recurrent HNC treated with re-irradiation was analyzed. Dysphagia following the second radiation course was dichotomized as grade ≥ 2 versus grade < 2 according to CTCAE criteria. Clinical features included tumor stage at re-RT, re-RT prescription dose, prior prescription dose, interval between the first and second courses, and the presence of dysphagia following the first radiation course. Dosimetric features were derived from cumulative dose distributions, with doses converted to equivalent dose in 2-Gy fractions (EQD2) to account for differences in fractionation. A logistic regression model (LR) was trained as the primary predictive model, with explainable boosting machine and decision tree models were trained for comparison. Model performance was evaluated using five-fold cross-validation and area under the receiver operating characteristic curve (AUC).

Fig 2. Feature importance of the logistic regression model for predicting dysphagia after head and neck re-irradiation, ranked by mean absolute weighted coefficients.

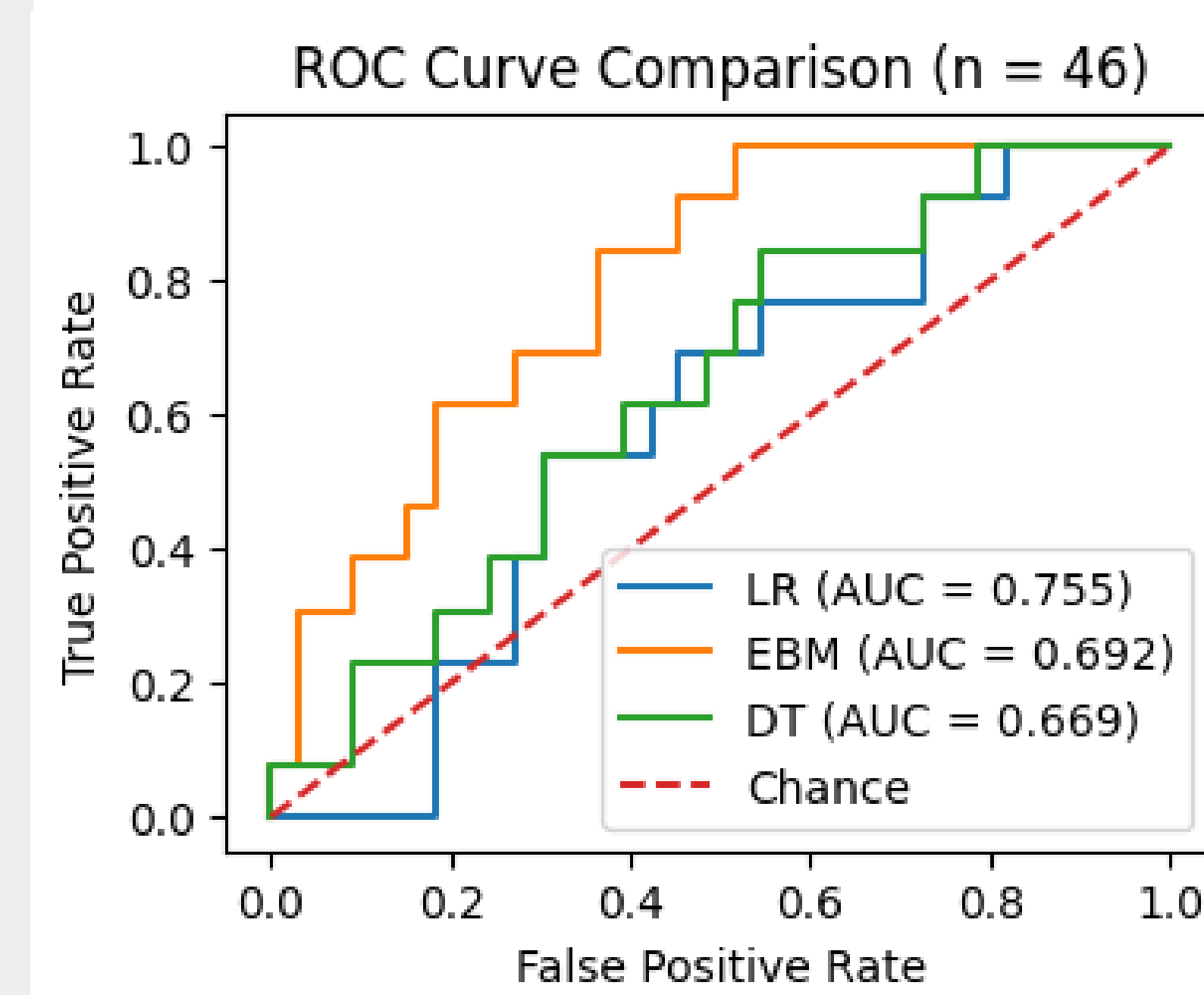
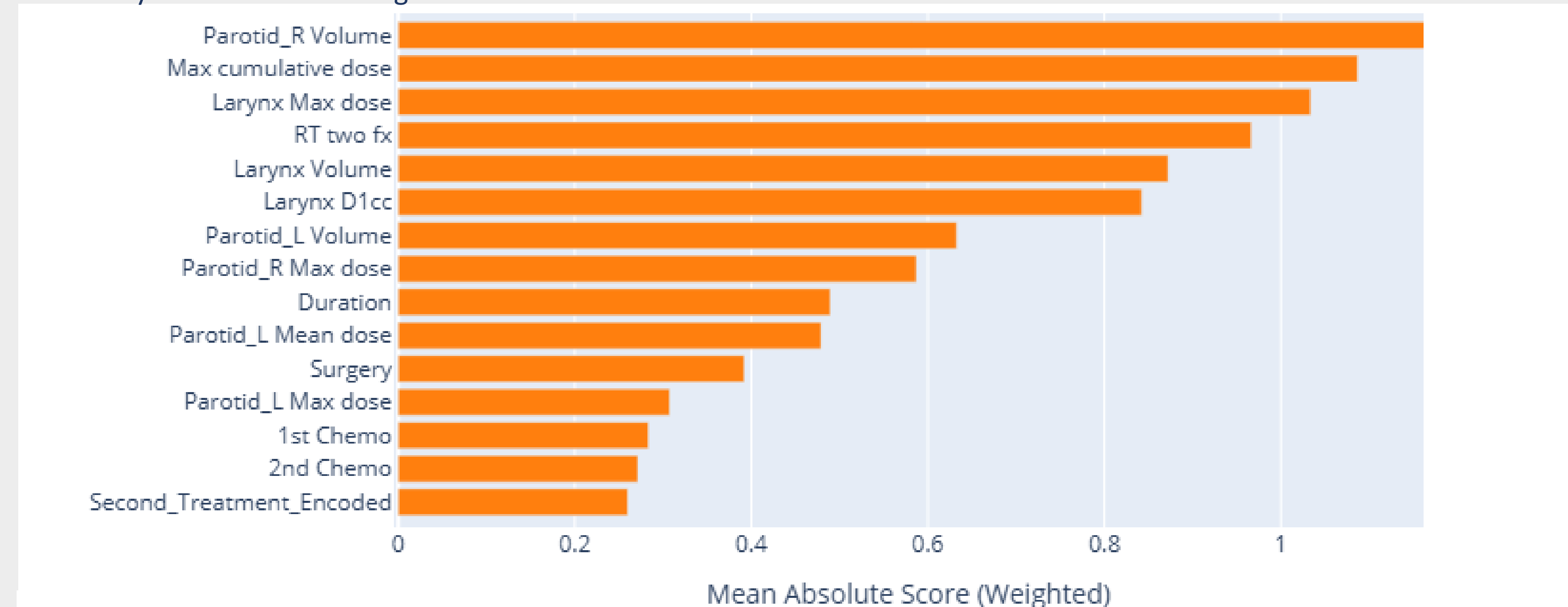


Fig 1. Receiver operating characteristic (ROC) curve comparison of logistic regression (LR), explainable boosting machine (EBM), and decision tree (DT) models for prediction of dysphagia after head and neck re-irradiation.

CONCLUSIONS

Interpretable modeling achieved clinically meaningful predictive performance for dysphagia after HNC re-irradiation and identified key predictors that align with prior clinical evidence.

These results support the clinical relevance of cumulative dose to salivary and laryngeal structures and highlight the potential of transparent models to guide patient selection, optimize organ-at-risk dose sparing, and demonstrate that clinically interpretable AI models can support prior knowledge–guided HNC re-irradiation planning.